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(21) International Application Number: PCT/US99/24481 (22) International Filing Date: 20 October 1999 (20.10.99) (30) Priority Data: 60/105,530 22 October 1998 (22.10.98) US (71)(72) Applicants and Inventors: GARDELLA, Thomas, J. [US/US]; 1045 Greendale Avenue, Needham, MA 02492 (US). KRONENBERG, Henry, M. [US/US]; 48 Hastings Road, Belmont, MA 02178 (US). POTTS, John, T., Jr. [US/US]; 129 Chestnut Street, Newton, MA 02165 (US). JÜPPNER, Harald [DE/US]; 38 Holyoke Street, #2, Boston, MA 02116 (US). (74) Agent: LUDWIG, Steven, R.; Sterne, Kessler, Goldstein & Fox P.L.L.C., Suite 600, 1100 New York Avenue, N.W., Washington, DC 20005-3934 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(54) Title: BIOACTIVE PEPTIDES AND PEPTIDE DERIVATIVES OF PARATHYROID HORMONE (PTH) AND PARATHYROID HORMONE-RELATED PEPTIDE (PTHrP)			
(57) Abstract  Novel parathyroid hormone peptide (PTH) and parathyroid hormone related peptide (PTHrP) or derivatives thereof which are biologically active are disclosed, as are pharmaceutical compositions containing said peptides, and synthetic and recombinant methods for producing said peptides. Also disclosed are methods for treating mammalian conditions characterized by decreases in bone mass using therapeutically effective pharmaceutical compositions containing said peptides. Also disclosed are methods for screening candidate compounds of the invention for antagonistic or agonistic effects on parathyroid hormone receptor action. Also disclosed are diagnostic and therapeutic methods of said compounds.			

activity. Such derivatives might be achieved through lactam cyclization, disulfide bonds, or other means known to a person of ordinary skill in the art.

Among the preferred embodiments are those compounds which may serve as agonists of the PTH-1/PTH-2 receptor. In particular, preferred embodiments are those compounds where  $X_{01}$  is Ala;  $X_{02}$  is Ile;  $X_{03}$  is Met;  $X_{04}$  is Asn;  $X_{05}$  is Leu; and  $X_{06}$  is His. The amino acid sequence of this preferred embodiment is thus AlaValSerGluIleGlnLeuMetHisAsnLeuGlyLysHis (SEQ ID NO: 5) or derivatives thereof.

Another set of the preferred embodiments are those compounds having a five amino acid deletion at the carboxy terminus of SEQ ID NO: 1 where  $X_{01}$  is Ala;  $X_{02}$  is Ile; and  $X_{03}$  is Met. The amino acid sequence of this preferred embodiment is thus AlaValSerGluIleGlnLeuMetHis (SEQ ID NO: 6) or derivatives thereof.

Another set of preferred embodiments are those compounds where  $X_{01}$  is Ala;  $X_{02}$  is Ile;  $X_{03}$  is Leu;  $X_{04}$  is Asp;  $X_{05}$  is Lys; and  $X_{06}$  is Ser. The amino acid sequence of this preferred embodiment is thus AlaValSerGluIleGlnLeuLeuHisAspLysGlyLysSer (SEQ ID NO: 2) or derivatives thereof.

Another set of preferred embodiments are those compounds having a five amino acid deletion at the carboxy terminus of SEQ ID NO: 1 where  $X_{01}$  is Ala;  $X_{02}$  is Ile; and  $X_{03}$  is Leu. The amino acid sequence of this preferred embodiment is thus AlaValSerGluIleGlnLeuLeuHis (SEQ ID NO: 7) or derivatives thereof.

Another set of preferred embodiments are those compounds having a five amino acid deletion at the carboxy terminus of SEQ ID NO: 1 where  $X_{01}$  is Ala;  $X_{02}$  is His; and  $X_{03}$  is Leu. The amino acid sequence of this preferred embodiment is thus AlaValSerGluHisGlnLeuLeuHis (SEQ ID NO: 8) or derivatives thereof.

Another set of the preferred embodiments are those compounds where  $X_{01}$  is Ser;  $X_{02}$  is His;  $X_{03}$  is Leu;  $X_{04}$  is Asp;  $X_{05}$  is Lys; and  $X_{06}$  is Ser. The amino acid sequence of this preferred embodiment is thus SerValSerGluHisGlnLeuLeuHisAspLysGlyLysSer (SEQ ID NO: 9) or derivatives thereof.

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